EXPERIMENTAL RESULTS

Part I: Animal experiments

1. In figure 1, it becomes obvious that BVDU when administered alone has no influence on the growth of tumors of rats. The tumors under influence of BVDU rather grow faster as compared without treatment.

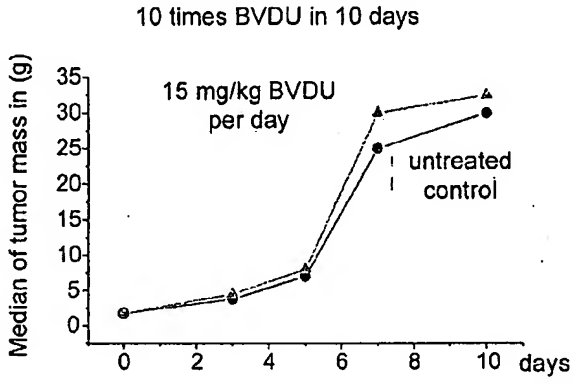

Figure 1: Indication that BVDU, when administered alone, has no effect.

2. The effect of chemotherapy without a "recovery"-effect is demonstrated with the following treatment scheme. BVDU is always administered at the same time together with Cisplatin (CIS):

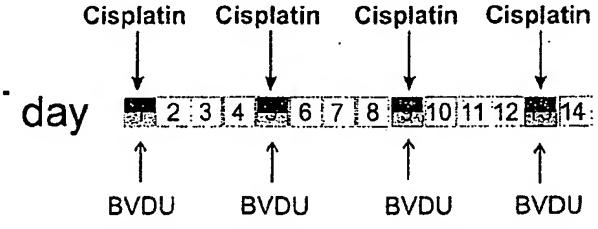

Figure 2a: Treatment scheme CIS + BVDU

Figure 2b shows the effect of BVDU when exclusively administered at the same day as the cytostatic.

No BVDU during the "recovery"-phase

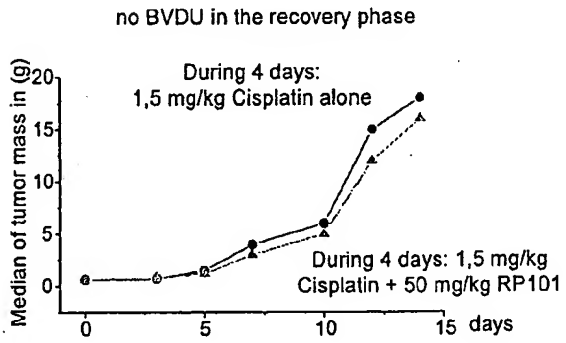

Figure 2b: Indication that BVDU, when administered alone together with CIS, only shows slight effects.

When BVDU exclusively is administered on the same day as the cytostatic agent, it only exhibits a slight increased effect. In these experiments, the dosage of BVDU exceeded 50 mg/kg, thus exceeding the standard dosage of 15 mg/kg by far.

3) In example 4 of the patent application (Doxorubicin, DOX), the "recovery"-phase in vivo was not only for one day, but the "recovery"-phase with this BVDU treatment was 6 times every day:

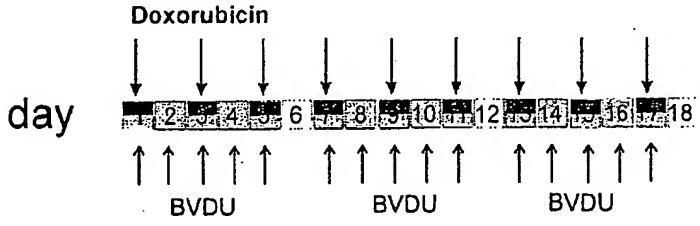

Figure 3a: Treatment scheme DOX + BVDU

In figure 3, the effect of this administering of BVDU in the "recovery"-phase is demonstrated.

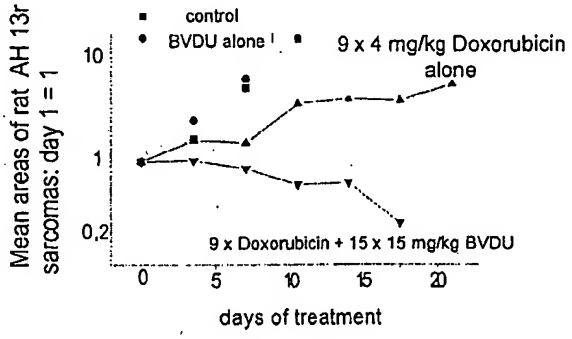

Figure 3b: Indication that administering of BVDU during the "recovery"-phase alternating alone and together with DOX has a strong effect. The effect of BVDU is extraordinary high also if the "recovery"-phase always lasts only one day.

4) When the "recovery"-phase is increased to 4 x 3 and 2 days, respectively, the following dosing scheme is applied:

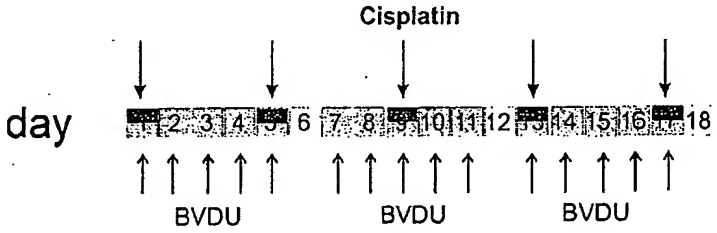

Figure 4a: Treating scheme CIS + BVDU

The effect of this treatment is demonstrated in figure 4b:

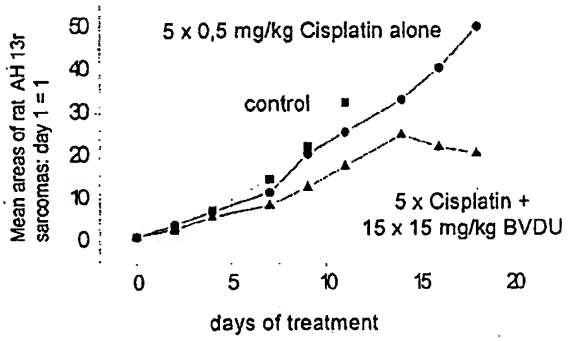

Figure 4B: Indication that administering of BVDU in the "recovery"-phase alternatingly alone and than 3 days together with CIS has a high effect.

The effect of BVDU is again very high, in particular, if compared to the combinative CIS + BVDU treatment (figure 2).

5) Elongation of the treatment time in the "recovery"-phase is only possible with Endoxan, because it exhibits a long-term-effect:

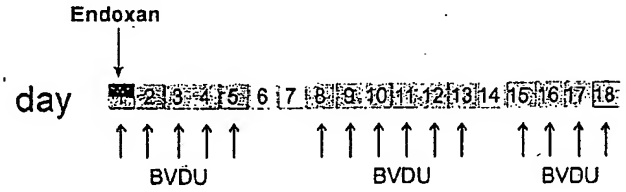

Figure 5a: Treatment Scheme Endoxan + BVDU

The effect of a 14-day treatment with BVDU in the "recovery"-phase is illustrated in figure 5b.

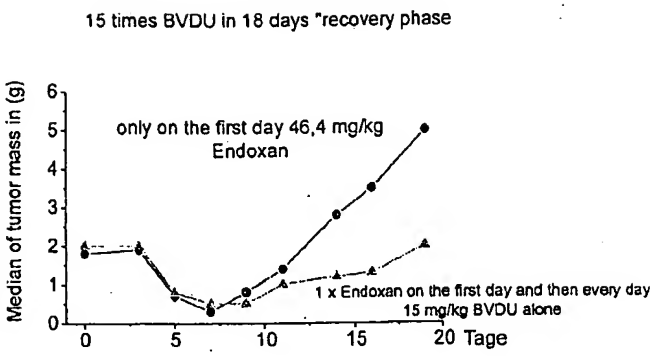

Figure 5b: Indication that a 15-time administering of BVDU alone in the "recovery"-phase together with the one-time treatment together with Endoxan only at the beginning of treatment has a significant effect.

This is the best example for the effect of BVDU in the "recovery"-phase. In summary, it can be stated that different dosage schemes of BVDU dependent on the cytostatic agent can be applied. The "recovery"-phase can last 6 times within one day to 1 time within fourteen days.

Basing on these findings, treatment schemes in clinical tests have been developed as practical applications:

Part II: Clinical studies

BVDU demonstrates significant effects in two clinical studies with Pankreas cancer patients. BVDU is administered during and after the chemotherapy. The co-treatment with BVDU increases the median survival times of Pankreas cancer patients by approximately the factor 2. A therapy thus is more successful as any other method of treatment described before.

1) Effectiveness of BVDU in a clinical study with 13 Pankreas cancer patients which were treated with Gemcitabine + Cisplatin + BVDU.

2 x 4 days "recovery" treatment (RP101 = BVDU):

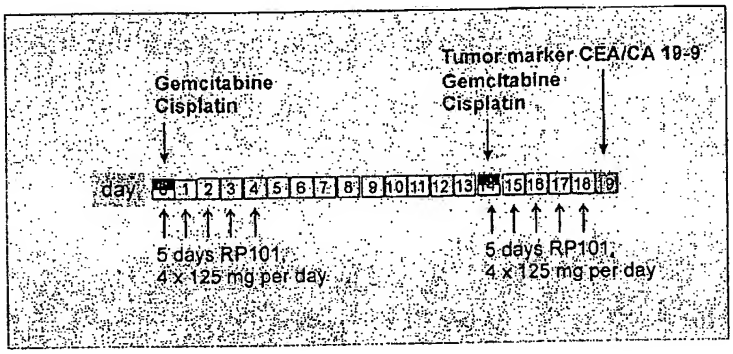

Figure 6a: Treatment scheme GEM + CIS + BVDU

In figure 6b, the surviving rate according to Kaplan-Meier is illustrated. The chances that patients with metastatic Pankreas carcinoma are healed, are approximately zero. Every step indicates a death of a patient, every x a surviving patient.

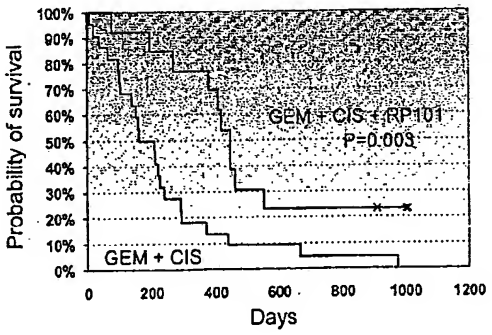

Figure 6b: Indication that BVDU when administered in the "recovery"-phase 4 times alone and only in the

beginning of the treatment together with GEM + CIS has a significant effect.

Result of phase-II-study with 13 patients: The treatment was the administering of BVDU in combination with Gemcitabine + Cisplatin (red line). The control group only was treated with Gemcitabine + Cisplatin (black line).

Result: The survival time according to the RP101-co-treatment was more than doubled.

2) Effectivity of BVDU in a clinical study with 21 Pankreas- cancer patients, which were treated with Gemcitabine + BVDU.

3 x 3 days "recovery" treatment (RPi01 = BVDU):

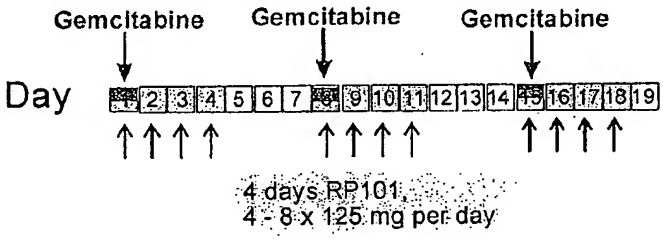

Figure 7a: Treating scheme GEM + BVDU

Figure 7b illustrates the survival rate according to Kaplan-Meier. Every step indicates a death of a patient, every x a surviving patient.

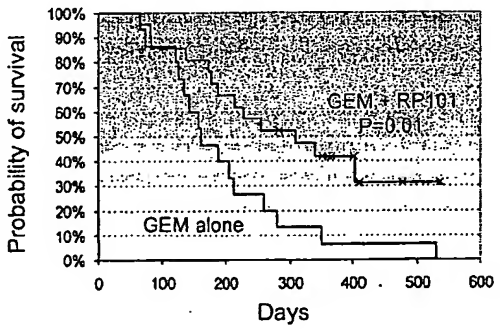

Figure 7b: Indication that the administering of BVDU during the "recovery"-phase 3 times alone and only in the beginning of the treatment one time together with GEM has a strong effectivity.

Result of this phase-II-study with 21 patients: The treatment was accomplished by increasing dosages of BVDU in a combination with Gemcitabine (red line). The control group was treated with Gemcitabine alone (black line).

Result: The survival time was approximately doubled by co-treatment with RP101.

Literature

Fahrig, R., Heinrich, J.C., Nickel, B., Wilfert, F., Leisser, C., Krupitza, G., Praha, C., Sonntag, D., Fiedler, B., Scherthan, H., and Ernst, H., „Inhibition of induced chemoresistance by co-treatment with (E)-5-(2-bromovinyl)-2'-deoxyuridine (RP101). Cancer Res. 63 (2003) 5745 -5753.

Fahrig, R., Quietzsch, D., Heinrich, J-C., Heinemann, V., Boeck, S., Schmid, R.M., Praha, C., Liebert, A., Sonntag, D., Krupitza, G., and Haenel, M., „RP101 improves the efficacy of chemotherapy in pancreas carcinoma cell lines and pancreatic cancer patients. Anti-Cancer Drugs 17, 1045-1056, 2006.